Review

Major bacterial diseases in aquaculture and their vaccine development

Julia W. Pridgeon* and Phillip H. Klesius

Address: Aquatic Animal Health Research Unit, USDA-ARS, 990 Wire Road, Auburn, AL 36832, USA.

***Correspondence:** Julia W. Pridgeon. Email: Julia.Pridgeon@ars.usda.gov

Received: 7 May 2012
Accepted: 27 July 2012

doi: 10.1079/PAVSNNR20127048

The electronic version of this article is the definitive one. It is located here: http://www.cabi.org/cabreviews

Abstract

Aquaculture is emerging as the fastest growing food-producing industry in the world because of the increasing demand for food fish consumption. However, the intensive culture of food fish has led to outbreaks of various bacterial diseases, resulting in annual economic losses to the aquaculture industry estimated at billions of dollars worldwide. Feeding infected fish with antibiotic-medicated food is a general practice but has led to antibiotic resistance development in bacterial pathogen, resulting in a higher dose requirement for effective control, a matter of increasing public concern. Therefore, alternatives to antibiotics that give similar or enhanced protection to aquatic animals are urgently needed. Various vaccines have been developed recently to combat bacterial diseases in aquaculture. The purpose of this review is to summarize the major bacterial pathogens in aquaculture and the development of vaccines as alternatives to antibiotics to protect aquatic animals from these bacterial diseases.

Keywords: Aquaculture, Attenuated, Bacteria, Disease, Vaccine

Review Methodology: United States Department of Agriculture National Agricultural Library's DigiTop Navigator platform was used to search the following databases: AGRICOLA, AGRIS, BIOSIS, CAB Abstracts, Fish, Fisheries & Aquatic Biodiversity Worldwide, Food Science and Technology Abstracts, MEDLINE, Wildlife & Ecology Studies Worldwide and Zoological Record (keyword search terms used: vaccine, bacteria, attenuated, aquaculture). In addition, references from the articles obtained by this method were used to check for additional relevant material.

Aquaculture as the Fastest Growing Food-Producing Industry

Aquaculture is also called 'underwater agriculture' [1]. There is an ever-increasing human population and consequent demand for food, but significant expansion of the traditional land-food production systems (such as plant agriculture, poultry, cattle/goat/pig farming, etc.) is limited by the fact that the earth has only 30% land coverage. To provide enough food for the rapidly growing human population, we need to utilize the remaining 70% area under water for food production [1]. Worldwide, the aquaculture industry has grown at an average rate of 8.9% per year since 1970, compared with a 1.2% growth rate of capture fisheries and 2.8% growth rate of terrestrial farmed meat production over the same period [2]. According to the 2010 FAO review on world fishery production [3], the capture production system has maintained similar level at 90 million tonnes for more than a decade [4], whereas the aquaculture production of fisheries has increased from 34.6 million tonnes in 2001 to 55.7 million tonnes in 2009 [3]. The value of aquaculture production was estimated at $105.3 billion in 2009 [2]. China remains as the leading force contributing to the increase of world total fishery production [4].

Major Bacterial Diseases Affecting Aquaculture

Notwithstanding the fact that aquaculture is the fastest growing food-production industry in the world the sector is plagued by diseases. The annual economic loss to the aquaculture industry through diseases is estimated to be billions of US dollars worldwide [5]. Major pathogens that are affecting the aquaculture industry include: bacteria [6–9], fungi [10, 11], viruses [12–15] and parasites

[16, 17]. Given that bacteria can survive well in aquatic environment independently of their hosts, bacterial diseases have become major impediments to aquaculture, especially when water temperature is warm [18]. Thus far, bacterial species belonging to at least 13 genera have been reported to be pathogenic to aquatic animals, including: (1) Gram-negative bacteria such as *Aeromonas*, *Edwardsiella*, *Flavobacterium*, *Francisella*, *Photobacterium*, *Piscirickettsia, Pseudomonas*, *Tenacibaculum*, *Vibrio* and *Yersinia*; and (2) Gram-positive bacteria such as *Lactococcus*, *Renibacterium* and *Streptococcus* [18]. Major pathogenic Gram-negative and Gram-positive bacterial species reported in disease outbreaks are summarized in Tables 1 and 2, respectively.

Fresh-water cultured fish as well as marine fish are devastated by bacterial diseases, including tilapia, catfish, carp, trout, salmon, bass, perch, sturgeon and eel. The annual economic loss associated with three bacterial fish pathogens (*Aeromonas hydrophila*, *Yersinia ruckeri* and *Vibrio fluvialis*) between 1990 and 1992 in China was estimated at more than $120 million [168]. Since the value of aquaculture production was estimated at $105.3 billion in 2009 [2], the global economic impact of bacterial diseases on aquaculture production would be within the range of hundreds of millions to billions of dollars annually.

Control of Bacterial Diseases in Aquaculture

To control bacterial diseases, feeding infected fish with antibiotic-medicated food is a general practice. However, this is usually expensive and may be ineffective because sick fish may remain off feed. In addition, frequent use of antimicrobial compounds has led to the development of resistance to antimicrobial compounds in pathogens, posing serious challenges to health and national security [169]. Resistance can arise in disease-causing bacteria, rendering life-saving antimicrobial compounds ineffective. Furthermore, diseases caused by antibiotic-resistant bacteria are difficult to treat, and there are only a few new antimicrobial compounds in the drug development pipeline. Therefore, alternatives to antimicrobial compounds that give similar or enhanced protection to aquatic animals are urgently needed. An integrated approach that considers not only the pathogen but also the host and the environment will be the most effective method in the long-term to improve aquatic animal health. From the pathogen perspective, besides using antimicrobial compounds, alternative methods in integrated management include: (1) using pathogen-specific bacteriophages; (2) using short-chain fatty acids and polyhydroxyalkanoates to inhibit the growth of bacteria; and (3) using compounds to inhibit virulence gene expression or interrupt the signal transduction pathways of the pathogens [170, 171]. From the environmental perspective of integrated management, good hygiene such as quarantine and disinfection to optimize water quality is important [171]. From the host perspective, it is important to: (1) provide quality feed; (2) prevent stress; (3) improve the breeding stock's disease resistance ability; and (4) adopt the use of immunostimulants or vaccines to improve host immunity [171]. The use of vaccine has been proven to be highly effective in controlling diseases in the salmon industry in Europe, America and Japan [172]. Vaccines have been used in fish, in particular the salmon industry, for approximately 30 years. Vaccination of salmon has dropped the industrial use of antibiotics to a mere fraction of its original use. For example, in 1987, approximately 50,000 kg of antibiotics was used in Norway to control fish diseases (mostly *Vibrio* spp.) in salmon prior to the widespread use of vaccines [173]. However, by 1997, when an efficacious oil-adjuvant vaccine was extensively used, antibiotic usage had dropped to less than 1000–2000 kg, concurrent with a threefold increase in fish production (Figure 1) [173]. In the following paragraphs, the recent development of vaccines to combat the major bacterial diseases in aquaculture will be reviewed.

Types of Bacterial Vaccines

In general, there are six types of bacterial vaccines: (1) bacterins (killed bacteria) such as the *Aeromonas salmonicida* bacterin vaccine that is currently available in the USA; (2) attenuated live bacterial vaccine such as the attenuated live *Edwardsiella ictaluri* vaccine that is commercially available in the USA; (3) toxoid vaccine containing inactivated bacterial toxins rather than the whole bacteria; (4) subunit vaccine such as a protein subunit of the bacterium, where instead of an inactivated or attenuated whole bacterium to stimulate the immune system, a fragment or a subunit of the bacterium is used to stimulate the immune response; (5) conjugate vaccine by conjugating certain membrane proteins of bacteria to other proteins to make the bacterial proteins recognizable, thereby inducing immune response; and (6) experimental vaccines such as DNA vaccines or recombinant vector vaccine. Of the six types of bacterial vaccines, the first two types are commonly used in aquaculture. Modified live vaccines containing live bacteria usually survives and replicates within the host, therefore stimulating a stronger cellular immune response and conferring a longer protection compared with killed vaccines.

Vaccine Development Status for Major Bacterial Diseases in Aquaculture

Currently, eight bacterial fish vaccines are licensed for use in the USA (http://www.aphis.usda.gov/animal_health/vet_biologics):

(1) *A. salmonicida* vaccine (bacterin);
(2) *Arthrobacter* vaccine (live culture);

Table 1 Summary of pathogenic Gram-negative bacteria and their hosts reported in literature

Pathogen	Disease	Host of pathogen
Aeromonas hydrophila	Motile aeromonads septicaemia	Catfish [19], carp [20, 21], trout [22, 23], eel [24], sturgeon [25], tilapia [26] and bass [27]
Aeromonas salmonicida	Furunculosis	Salmon [28, 29], trout [30], flounder [31], turbot [32], carp [33], tilapia [33] and sole [31]
Chryseobacterium sp.	Chryseobacteriosis	Salmon [34, 35] and trout [35]
Edwardsiella ictaluri	Enteric septicaemia of catfish	Catfish [36–39]
Edwardsiella tarda	Edwardsiellosis or putrefactive disease	Turbot [40, 41], flounder [42, 43], carp [44], catfish [45], eel [45, 46] and tilapia [47, 48]
Flavobacterium columnare	Columnaris	Carp [49, 50], trout [51, 52], perch [53], tilapia [54, 55], catfish [56] and salmon [39]
Flavobacterium johnsonae	False columnaris	Barramundi [57]
Flavobacterium psychrophilum	Flavobacteriosis or rainbow trout fry syndrome	Trout [58, 59]
Flavobacterium branchiophilum	Bacterial gill disease	Trout [60]
Francisella spp.	Francisellosis	Tilapia [61] and hybrid striped bass [62]
Moritella viscosa	Winter ulcer disease	Salmon [63, 64]
Photobacterium spp. (formerly *Pasteurella* spp.)	Pasteurellosis	Sturgeon [65], hybrid striped bass [66], seabream [67–69], yellowtail [70], sea bass [71], snakehead [72], tuna [73] and cobia [74]
Piscirickettsia salmonis and *Piscirickettsia*-like organism	Piscirickettsiosis or rickettsial septicaemia	Salmon [75], trout [75] and tilapia [76, 77]
Pseudomonas spp.	Pseudomonads septicaemia or red spot disease	Seabream [78], trout [79], eel [80], rabbitfish [81], catfish [82], eel [83], shrimp [84] and salmon [85]
Tenacibaculum maritimum	Tenacibaculosis	Sole [86] and turbot [87]
Vibrio spp.	Vibrosis	Croaker fish [88], puffer fish [89], grouper [90], cod [91], shrimp [92, 93], big-scale sand smelt [94], flounder [95], abalone [96], seabream [97, 98], turbot [99, 100], sole [101], red drum [102], cobia [103], eel [104, 105], salmon [106], sweetfish [107], sheatfish [108] and catfish [109]
Yersinia ruckeri	Yersiniosis or enteric redmouth disease	Trout [110–112], tilapia [113] and salmon [114, 115]

Table 2 List of pathogenic Gram-positive bacteria and their hosts reported in literature

Pathogen	Disease	Host of pathogen
Lactococcus garvieae (formerly *Enterococcus seriolicida*)	Lactococcosis	Yellowtail [116, 117], trout [118–120], rockfish [121] and mullet [122]
Nocardia sp.	Nocardiosis	Tigerfish [123], snakehead [124, 125], croaker [126, 127], mullet [128], seabass [129], largemouth bass [130, 131], gourami [132] and yellowtail [133]
Renibacterium salmoninarum	Bacterial kidney disease	Trout [134] and salmon [135, 136]
Staphylococcus spp.	Staphylococcosis	Trout [137], tilapia [138], carp [139], perch [140], seabream [141, 142] and yellowtail [142]
Streptococcus agalactiae	Streptococcosis	Tilapia [143, 144] Grouper [145], mullet [146] and pomfret [147]
Streptococcus ictaluri	Streptococcosis	Catfish [148]
Streptococcus iniae	Streptococcosis	Tilapia [149], seabream [150], red porgy [151], trout [151], flounder [152], barramundi [153], rabbitfish [154], hybrid striped bass [155], yellowtail [156] and catfish [157]
Streptococcus dysgalactiae	Streptococcosis	Sturgeon [158], amberjack [159, 160] and yellowtail [160]
Streptococcus parauberis	Streptococcosis	Turbot [161] and flounder [162]
Streptococcus phocae	Streptococcosis	Salmon [163]
Vagococcus salmoninarum	Coldwater 'streptococcosis'	Trout [164, 165]
Weissella sp.	Haemorrhagic septicaemia	Trout [166, 167]

(3) *A. salmonicida–Vibrio anguillarum–Vibrio ordalii–Vibrio salmonicida* (*Aliivibrio salmonicida*) vaccine (bacterin);
(4) *Flavobacterium columnare* vaccine (bacterin);
(5) *Y. ruckeri* vaccine (bacterin);
(6) *V. anguillarum–V. ordalii* vaccine (bacterin);
(7) *E. ictaluri* vaccine (avirulent live culture);
(8) *F. columnare* vaccine (avirulent live culture).

The eight vaccines are licensed for use in aquaculture practices for protection against bacterial diseases. However, vaccines are usually licensed for specific fish species. Therefore, license of certain vaccine for one fish species may not be used to protect another fish species, although the pathogen might be the same. For example, the *F. columnare* bacterium vaccine is currently licensed for use only in catfish.

Worldwide, vaccines have been developed and commercially available to treat at least 18 bacterial infections [173, 175, 176]:

(1) vibriosis caused by *V. anguillarum* (formerly *Listonella anguillarum*) or *V. ordalii* in salmonids, cod, halibut, seabass, seabream, amberjack and yellowtail;
(2) coldwater vibriosis caused by *V. salmonicida* in salmonids;
(3) winter ulcer disease or wound disease caused by *Moritella viscosa* in salmonids;
(4) furunculosis caused by *A. salmonicida* subsp. *salmonicida* in salmonids;
(5) atypical *A. salmonicida* caused by *A. salmonicida* in salmonids;
(6) yersiniosis caused by *Y. ruckeri* in salmonids;
(7) piscircickettsiosis caused by *Piscirickettsia salmonis* in salmonids;
(8) bacteria gill disease caused by *Flavobacterium branchiophilum* in salmonids and carp;
(9) flavobacteriosis caused by *Flavobacterium psychrophilum* in salmonids;
(10) columnaris caused by *F. columnare* in channel catfish and salmonids;
(11) enteric septicaemia of catfish caused by *E. ictaluri* in catfish;
(12) Edwardsiellosis or putrefactive disease caused by *Edwardsiella tarda* in tilapia;
(13) bacterial kidney disease caused by *Renibacterium salmoninarum* in salmonids;
(14) lactococcosis caused by *Lactococcus garvieae* in rainbow trout, amberjack and yellowtail;
(15) Pasteurellosis caused by *Photobacterium damselae* subsp. *piscicida* in seabream, seabass, amberjack and yellowtail;
(16) streptococcosis caused by *Streptococcus iniae* or *Streptococcus phocae* in tilapia, seabass and salmonids;
(17) wound disease or winter ulcer disease caused by *M. viscosa* in salmon; and
(18) streptococcosis/lactococcosis caused by *S. iniae* and *L. garvieae* in trout.

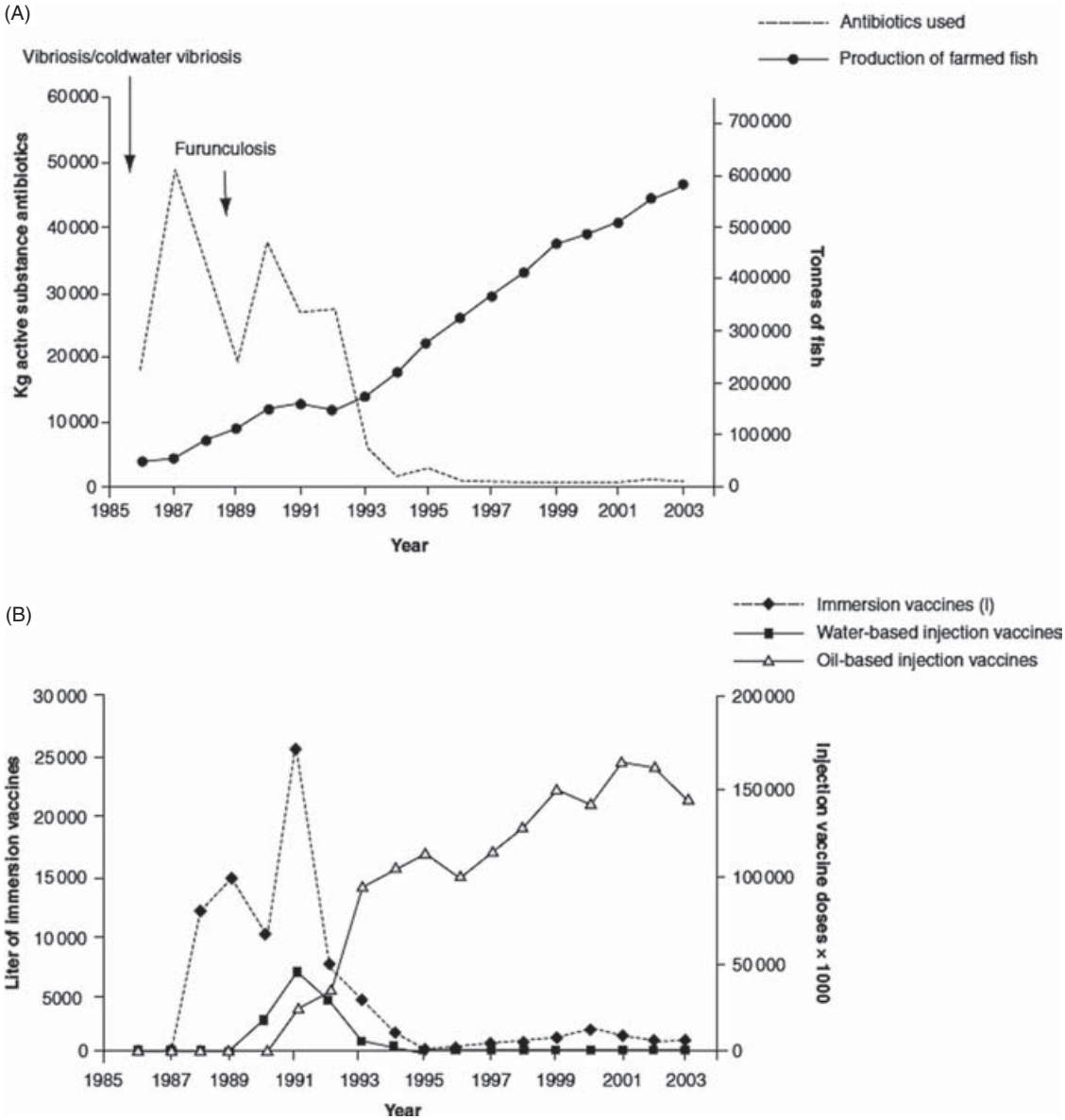

Figure 1 The use of the antibiotics (A) and different types of vaccines (B) during the growth of Norweigian aquaculture industry from 1986 to 2003. Information obtained from Sommerset *et al*. [173]

Although vaccines are commercially available for protection against 18 diseases mentioned above, there are other important diseases in aquaculture, including motile aeromonads septicaemia, chryseobacteriosis, Francisellosis, pseudomonads septicaemia, nocardiosis, staphylococcosis, streptococcosis caused by *Streptococcus agalactiae*, and other emerging diseases, for which vaccines are not yet available. The causative agents of these diseases and their vaccine development status are summarized below:

(1) Motile aeromonad septicaemia (MAS) caused by *A. hydrophila*. Although usually considered as a secondary pathogen associated with disease outbreaks, *A. hydrophila* could also become a primary pathogen, causing outbreaks in fish farms with high mortality rates and severe economic losses to the aquaculture industry [174, 177–181]. In West Alabama of USA, disease outbreaks caused by *A. hydrophila* in 2009 and 2010 caused an estimated loss of more than $3 million annually [182, 183]. Virulence studies have revealed that the 2009 West Alabama isolates of *A. hydrophila* are highly virulent to channel catfish, with LD_{50} values as low as 2×10^2 CFU/fish by intraperitoneal injection [183]. MAS disease caused by *A. hydrophila* such as the 2009 West Alabama isolate could be very acute, causing high mortality within 24 h [182, 183]. Therefore, vaccines are urgently needed to prevent MAS. The most extensively studied *A. hydrophila* vaccines are bacterins consisting of formalin or heat-killed

bacteria of pathogenic *A. hydrophila* strains [184–186]. In addition, recombinant protein vaccines such as *A. hydrophila* outer membrane proteins and bacterial lysate have been demonstrated to elicit protection against *A. hydrophila* challenges in laboratory studies [187–190]. Furthermore, live attenuated vaccines such as *aroA* mutant and transposon Tn916-generated mutant have been reported to confer significant protection against homologous *A. hydrophila* challenge [191, 192]. However, it is well known that *A. hydrophila* is very heterogeneous biochemically and serologically, thus presenting the biggest obstacle in developing effective commercial vaccine against *A. hydrophila* [188, 193]. To prevent future disease outbreaks caused by *A. hydrophila*, a vaccine that could offer protection against multiple serotypes from various regions is urgently needed.

(2) Chryseobacteriosis or salmon skin syndrome caused by *Chryseobacterium* sp. Although members of *Chryseobacterium* are not relevant pathogens for domestic animal species, they have been associated with diseases of freshwater and marine fish [34, 35, 194]. In addition, *Chryseobacterium* sp. is reported to be the causative agent of salmon skin syndrome [195]. Therefore, vaccines are needed to protect fish from virulent isolates of *Chryseobacterium*.

(3) Francisellosis caused by *Francisella* sp. Within the last decade, *Francisella* sp. have been reported to cause high mortality in a wide range of diseased fish, including three-line grunt (*Parapristipoma trilineatum*) in Japan [196], hybrid striped bass (*Morone chrysops*× *Morone saxatilis*) in USA [197], cod (*Gadus morhua*) in Norway [198–200], tilapia (*Oreochromis* spp.) in Latin America, Costa Rica, UK and USA [61, 201–203], salmon (*Salmo salar*) in Chile [204] and giant abalone (*Haliotis gigantean*) in Japan [205]. More aquatic animals are possibly affected by *Francisella* bacteria because of their fastidious growth condition requiring specialized solid and liquid media containing cysteine and a source of iron, resulting in difficult culture and isolation. Francisellosis in fish develops in a similar fashion independent of host species. The common disease characteristic is the development of multi-organ granuloma and high morbidity [206]. *Francisella* can be transferred through live fish movement [207], making Francisellosis a significant threat to aquaculture operations. Experimentally, one deletion mutant of *Francisella asiatica* iglC has been evaluated as a live attenuated vaccine, which is able to offer significant protection against virulent *F. asiatica* infections in tilapia [208]. However, no vaccine is currently commercially available to protect fish against infections by *Francisella* bacteria.

(4) Pseudomonad septicaemia or red spot disease caused by *Pseudomonas* spp. *Pseudomonas* spp. are emerging fish pathogens responsible for high mortality and disease outbreaks in various fish species. *Pseuodomonas anguilliseptica* was first reported in Japanese eels (*Anguilla japonica*) affected by haemorrhagic septicaemia in Japan [209]. Subsequently, *Pseudomonas* spp. was recognized as the causative agents of red spot diseases in different aquatic animals, including European eel (*Anguilla anguilla*) in UK and the Netherlands [81, 85], Atlantic salmon (*S. salar*) [210], sea trout (*Salmo trutta*) [210], rainbow trout (*Salmo gairdneri*), whitefish (*Coregonus* sp.) in Finland [210], sea bream (*Sparus aurata*) in Spain [211, 212] and rainbow trout (*Oncorhynchus mykiss*) in Turkey [80]. In addition, when combined with parasite, *Pseudomonas* is responsible for over 70% mortality of sea bream in Egypt [79]. Pseudomonad septicaemia is characterized by high mortality related to a decrease in the water temperatures below 11–12°C [210]. The typical clinical sign is ulceration on the dorsal surface. To prevent diseases caused by *Pseudomonas* spp., different experimental vaccines have been used. Formalin-killed and heat-inactivated cells of *P. anguilliseptica* have been reported to offer protection in eels against virulent *Pseudomonas* infection [213, 214]. Bacterin against *P. anguilliseptica* was also able to provide protection to turbot (*Scophthalmus maximus*) for 12 weeks when tested in an experimental challenge trial [215]. However, no vaccine is currently commercially available to protect aquatic animals against *Pseudomonas* bacterial infections.

(5) Nocardiosis caused by *Nocardia* sp. *Nocardia* bacteria are aerobic, Gram-positive, branching, filamentous and rod-shaped. Although many *Nocardia* species are commonly found in soil and plants [216–218], which may be innocuous to human and animals, some *Nocardia* species are primary pathogen of human and animals [219–222]. Recently, *Nocardia* sp. has been isolated from various diseased aquatic animals, including three striped tigerfish (*Terapon jarbua*) [123], snakehead (*Ophiocephalus argus*) [124, 125], large croaker (*Pseudosciaena crocea*) [126], yellow croaker (*Larimichthys crocea*) [127], striped mullet (*Mugil cephalus*) [128], seabass (*Lateolabrax japonicus*) [129], largemouth bass (*Micropterus salmoides*) [130, 131], giant gourami (*Osphronemus goramy*) [132] and yellowtail (*Seriola quinqueradiata*) [133]. Nocardiosis is a systemic disease of fish where lesions are localized in the skin and several internal organs, with the presence of nodular lesions typical of granulomata [127]. An epizootic disease in large-mouth bass (*M. salmoides*) in a fresh water pond was reported to be caused by *Nocardia asteroides* in Taiwan in 1989, with an accumulative mortality of 30% (15 000 out of total 50 000 fish) within 1 month [131]. *Nocardia* sp. also caused 17.5% mortality (3500 out of 20 000 fish) within a month in pond cultured sea bass (*L. japonicus*) in Taiwan in 1997 [129]. In Zhejiang China, *Nocardia* sp. caused 35% mortality (180 000 out of 500 000) in pond-cultured snakehead (*Ophiocephalus argus*)

in 2006 [125]. Chemotherapy for nocardiosis has been ineffective partly because the tubercles formed in diseased fish prevents access and sequestrate the organisms from the drug effect [133]. Killed vaccines have been evaluated experimentally in yellowtail and largemouth bass. Although yellowtail immunized with formalin-killed cells (FKC) of *Nocardia seriolae* or FKC with Freund's Incomplete Adjuvant (FKC-FIA) showed humoural responses, no protective effect was observed in immunized yellowtail [223]. Similarly, when largemouth bass (*M. salmoides*) were immunized with FKC of four different strains of *N. seriolae*, specific antibody titres were increased significantly at 4 weeks after immunization. However, immunization with different strains with or without booster immunization failed to protect largemouth bass against challenges by virulent strains of *N. seriolae* [224]. On the other hand, when yellowtails (*S. quinqueradiata*) were vaccinated with live bacteria of *Nocardia soli* and *Nocardia fluminea* cells, slight protection against an artificial challenge with *N. seriolae* was observed [23]. In addition, fish that survived the *N. seriolae* infection showed complete resistance to the *N. seriolae* challenge [225], suggesting that live vaccines should be developed to protect aquatic animals against nocardiosis.

(6) Staphylococcosis caused by *Staphylococcus* spp. *Staphylococcus* bacteria are important opportunistic human pathogens and leading cause of a wide variety of diseases in humans and animals [226]. For example, *Staphylococcus aureus* is the aetiological agent responsible for a large extent of morbidity and mortality globally, in both hospital and community settings [227, 228]. Antibiotic resistance in *S. aureus* is a major clinical problem, in particular in infections caused by methicillin-resistant *S. aureus* (MRSA) [226]. In aquatic animals, three *Staphylococcus* species (*Staphylococcus epidermidis* [142], *S. aureus* [141] and *Staphylococcus warneri* [137]) have been reported as disease-causing agents. *S. epidermidis* was reported to be the causative agent of the epizootics in cultured yellowtail (*S. quinqueradiata*) and red sea bream (*Chrysophrys major*) in Japan between 1976 and 1977 [142]. *S. epidermidis* was responsible for the mass mortality of tilapia between 1992 and 1996 in Taiwan [138]. *S. aureus* was reported to be the causative agent of an eye disease during 1982 and 1983 in India, causing mortalities in silver carp, *Hypophthalmichthys molitrix* [227]. *S. warneri* is reported to be the causative agent of a disease outbreak in a rainbow trout farm during the spring of 1997 (May–June) in Spain [137]. The typical symptoms of staphylococcosis are exophthalmia and swollen lesion on the tail [142]. Currently no vaccine against *Staphylococcus* spp. is commercially available or experimentally tested in aquatic animals.

(7) Streptococcosis caused by *Streptococcus* sp. *Streptococcus* bacteria are important pathogens of both human and other animals. For example, *S. agalactiae* (group B *streptococcus*) is an important cause of disease in infants, pregnant women, elderly and immune-suppressed adults [229]. In addition, *S. agalactiae* is responsible for many cases of acute clinical mastitis in dairy animals [230, 231]. *S. agalactiae* also affects a variety of cultured and wild fish species in freshwater, estuarine and marine environments. These include tilapia [143, 144], grouper [145], mullet [146] and pomfret [147]. In August and September of 2001, *S. agalactiae* was responsible for a massive fish kill at the Kuwait Bay, killing over 2500 metric tonnes of wild mullet (*Liza klunzingeri*) [146]. In addition, *S. agalactiae* was reported to be the causative agent of disease outbreaks from 2007 to 2011 in Queensland, Australia in giant Queensland grouper (*Epinephelus lanceolatus*) [145]. No commercial vaccine against *S. agalactiae* is currently available in aquaculture. Experimentally, formalin-killed cells along with concentrated extracellular products (>3 kDa) of a single isolate of *S. agalactiae* have been reported to offer significant protection to 30 g tilapia, but not to 5 g tilapia, with a relative percent of survival (RPS) rate of 80% in vaccinated fish compared with non-vaccinated fish at 30 days post vaccination [232, 233]. However, the RPS dropped to 60, 55 and 46% at 47, 90 and 180 days post vaccination, respectively [234]. It was also reported that a formalin-killed *S. agalactiae* vaccine was able to increase the antibody titre in vaccinated fish compared with control fish. However, vaccination by either intraperitoneal injection or by a combination of intraperitoneal injection with oral booster vaccination (one and two doses per month) failed to protect Nile tilapia from *S. agalactiae* infections [235]. In addition, an experimental *S. agalactiae* biotype 1 (β-haemolytic) vaccine was reported to be able to offer protection against lethal challenges with both biotype 1 and biotype 2 (non-haemolytic) strains, whereas biotype II failed to offer protection against challenges with biotype 1 [236]. Recently, Merck Animal Health Inc. has obtained regulatory approval in Brazil to begin marketing AQUAVAC® Strep Sa, an inactivated oil-adjuvanted vaccine that provides protection against *S. agalactiae* infections in tilapia and other susceptible fish species. However, AQUAVAC® Strep Sa is only available by injection to fish weighing more than 15 g, which is rather labour-intensive. Besides *S. agalactiae*, *S. iniae* is also an important fish pathogen in aquaculture. Although bacterin vaccine is currently available in Asia to protect tilapia from *S. iniae* infection, it is not available for use in other parts of the world. *S. iniae* is responsible for a disease outbreak that killed 75% of hybrid tilapias (*Tilapia nilotica*×*Tilapia aurea*) in a Texas fish farm in USA in the early 1990s [237]. *S. iniae* is also the causative agent of disease outbreaks in seabream [150], red porgy [151], trout [151], flounder [152], barramundi

[153], rabbitfish [154], yellowtail [156] and catfish [157]. The most extensively studied *S. iniae* vaccines are bacterins [238, 239]. These formalin-killed *S. iniae* have been previously successfully used as vaccines to protect rainbow trout in Israel. However, recently it has been reported that these bacterins are unable to protect fish from infection by variant isolates (serotypes) of *S. iniae* [240, 241]. Other vaccines consisting of both formalin killed *S. iniae and* concentrated extracellular products of *S. iniae* have been reported to partially protect Nile tilapia (*Oreochromis niloticus* L.) from *S. iniae* infection [242–245]. Bacterins against *S. iniae* infection in tilapia are commercially available in Asia [179]. In addition to bacterins, live attenuated *S. iniae* strains defective in phosphoglucomutase and M-like protein have been reported to offer protection against homologous *S. iniae* challenge [246, 247]. However, it is not clear whether they offer protection against heterologous *S. iniae*. Recently, a highly efficacious attenuated *S. iniae* vaccine (ISNO) has been reported to protect tilapia at least 6 months against a virulent *S. iniae* strain [248]. In addition, ISNO is able to offer protection against heterologous virulent strains of *S. iniae* (F3CB, 102F1 K, 405F1 K, IF6 and ARS60) at 2-month post vaccination, with relative percent of survival of 78, 90, 100, 100 and 100%, respectively [248]. Furthermore, ISNO vaccine has a wide range of efficacious immunization dosage, with RPS values of 81, 94, 100, 100, 100 and 100 at vaccination dosage of 1×10^2, 1×10^3, 1×10^4, 1×10^5, 1×10^6 and 1×10^7 CFU/fish, respectively [248]. In addition to *S. agalactiae* and *S. iniae*, other *Streptococcus* bacteria are also emerging as important pathogens in aquaculture. For example, *Streptococcus dysgalactiae* is responsible for disease outbreaks in trout, sturgeon, amberjack and yellowtail [157–159], and *S. phocae* is the causative agent of repeated disease outbreaks in cage-farmed Atlantic salmon in Chile since 1999, with mortality up to 25% [160–162]. Currently, no vaccine is commercially available to protect fish from infections by *S. dysgalactiae* or *S. phocae*.

(8) Other emerging diseases. Besides the major diseases mentioned above, other emerging diseases can also be detrimental to the aquaculture industry, including the coldwater 'streptococcosis' caused by *Vagococcus salmoninarum* [163–165], and the haemorrhagic septicaemia caused by *Weissella* sp. [166, 167]. Vaccines have not yet been developed to protect fish from these emerging diseases either commercially or experimentally.

Conclusion

Aquaculture is the fastest growing food-producing industry. To provide sufficient food for the ever-increasing human population, protecting the aquaculture industry from diseases is a priority. To prevent bacterial diseases, using vaccines instead of antibiotics has been proven to be effective and beneficial. Although various vaccines have been developed to protect aquatic animals against various bacterial diseases, vaccines against multiple emerging diseases are still urgently needed for the aquaculture industry. In addition, majority of the vaccines available are bacterins which can only provide partial protection against certain strains for a limited time frame. Furthermore, most vaccines have to be delivered by injection, which is labour-intensive. Therefore, user-friendly (immersion or oral delivery) efficacious vaccines that can offer broader protection for a longer duration are urgently needed for the aquaculture industry.

Acknowledgements

We thank Drs Dehai Xu (USDA-ARS) and Victor Panangala (USDA collaborator) for critical reviews of the manuscript. This study was supported by the USDA/ARS CRIS project no. 6420-32000-024-00D. The use of trade, firm or corporate names in this publication is for the information and convenience of the reader. Such use does not constitute an official endorsement or approval by the United States Department of Agriculture or the Agricultural Research Service of any product or service to the exclusion of others that may be suitable.

References

1. Khan MA, Khan S, Miyan K. Aquaculture as a food production system: a review. Biology and Medicine 2011;3:291–302.
2. Subasinghe RP. Epidemiological approach to aquatic animal health management: opportunities and challenges for developing countries to increase aquatic production through aquaculture. Preventive Veterinary Medicine 2005;67:117–24.
3. Food and Agriculture Organization of the United Nations. FAO Yearbook: Fishery and Aquaculture Statistics. FAO, Rome; 2009. p. 12–3.
4. Food and Agriculture Organization of the United Nations. The State of World Fisheries and Aquaculture. FAO, Rome; 2010. p. 4–5.
5. Subasinghe RP, Bondad-Reantaso MG, McGladdery SE. Aquaculture development, health and wealth. In: Subasinghe RP, Bueno P, Phillips MJ, Hough C, McGladdery SE, Arthur JR, editors. Aquaculture in the Third Millennium. Technical Proceedings of the Conference on Aquaculture in the Third Millennium Bangkok: NACA and FAO; 2001. p. 167–91.
6. Frans I, Michiels CW, Bossier P, Willems KA, Lievens B, Rediers H. *Vibrio anguillarum* as a fish pathogen: virulence factors, diagnosis and prevention. Journal of Fish Diseases 2011;34:643–61.
7. Wang W. Bacterial diseases of crabs: a review. Journal of Invertebrate Pathology 2011;106:18–26.

8. Birkbeck TH, Feist SW, Verner-Jeffreys DW. *Francisella* infections in fish and shellfish. Journal of Fish Diseases 2011;34:173–87.

9. Jacobs JM, Stine CB, Baya AM, Kent ML. A review of mycobacteriosis in marine fish. Journal of Fish Diseases 2009;32:119–30.

10. Ramaiah N. A review on fungal diseases of algae, marine fishes, shrimps and corals. Indian Journal of Marine Sciences 2006;35:380–7.

11. Khoo L. Fungal diseases in fish. Seminars in Avian and Exotic Pet Medicine 2000;9:102–11.

12. Vega-Heredia S, Mendoza-Cano F, Sanchez-Paz A. The infectious hypodermal and haematopoietic necrosis virus: a brief review of what we do and do not know. Transboundary and Emerging Diseases 2012;59:95–105.

13. Ransangan J, Manin BO, Abdullah A, Roli Z, Sharudin EF. Betanodavirus infection in golden pompano, *Trachinotus blochii*, fingerlings cultured in deep-sea cage culture facility in Langkawi, Malaysia. Aquaculture 2011;315:327–34.

14. Oidtmann B, Stentiford GD. White spot syndrome virus (WSSV) concentrations in crustacean tissues – a review of data relevant to assess the risk associated with commodity trade. Transboundary and Emerging Diseases 2011;58:469–82.

15. Gomez-Casado E, Estepa A, Coll JM. A comparative review on European-farmed finfish RNA viruses and their vaccines. Vaccine 2011;29:2657–71.

16. Guo FC, Woo PT. Selected parasitosis in cultured and wild fish. Veterinary Parasitology 2009;163(3, Special Issue):207–16.

17. Brooker AJ, Shinn AP, Bron JE. A review of the biology of the parasitic copepod *Lernaeocera branchialis* (L., 1767) (Copepoda: Pennellidae). Advances in Parasitology 2007;65:297–341.

18. Klesius PH, Pridgeon JW. Live attenuated bacterial vaccines in aquaculture. In: Proceedings of the 9th International Symposium on Tilapia in Aquaculture; 2011. p. 18–26.

19. Pridgeon JW, Klesius PH. Molecular identification and virulence of three *Aeromonas hydrophila* isolates cultured from infected channel catfish during a disease outbreak in west Alabama (USA) in 2009. Diseases of Aquatic Organisms 2011;94:249–53.

20. Shome R, Shome BR, Mazumder Y, Das A, Kumar A, Rahman H, *et al.* Abdominal dropsy disease in major carps of Meghalaya: isolation and characterization of *Aeromonas hydrophila*. Current Science (Bangalore) 2005;88:1897–900.

21. Coz-Rakovac R, Popovic NT, Strunjak-Perovic I, Krca S, Grubacevic N. *Aeromonas hydrophila* outburst on carp (*Cyprinus carpio*, L.) after transfer to aquarium. Periodicum Biologorum 2000;102:293–6.

22. Ogara WO, Mbuthia PG, Kaburia HF, Sorum H, Kagunya DK, Nduthu DI, *et al.* Motile aeromonads associated with rainbow trout (*Onchorhynchus mykiss*) mortality in Kenya. Bulletin of the European Association of Fish Pathologists 1998;18:7–9.

23. Fuentes RJ, Pérez HJ. Isolation of *Aeromonas hydrophila* in the rainbow trout (*Oncorhynchus mykiss*). Veterinaria México 1998;29:117–9.

24. Timur M. An outbreak of a disease of farmed eel (*Anguilla anguilla*) due to *Aeromonas hydrophila* in turkey: histopathological and bacteriological studies. Veteriner Fakultesi Dergisi Ankara Universitesi 1983;30:361–7.

25. Zhao F, Cao J, Liu Q. Study on pathology and etiology of hemorrhagic septicemia in *Acipenser baerii*. Acta Hydrobiologica Sinica 2009;33:316–23.

26. Jiménez AP, Iregui CA, Figueroa J. *In vitro*/*in vivo* characterization and evaluation of *Aeromonas hydrophila* lipopolysacharides (LPS). Acta Biologica Colombiana 2008;13(2):147–62.

27. Plumb JA. Major diseases of striped bass and redfish. Veterinary and Human Toxicology 1991;33(Suppl 1):34–9.

28. St JB. Practical experience with furunculosis in an Atlantic salmon hatchery in Washington State. Bulletin of the Aquaculture Association of Canada 1992;(1):47–8.

29. Rottereng J, Stenmark A, Malmberg G. Control of furunculosis in fresh- and seawater farms in Norway. Parasites and Diseases in Natural Waters and Aquaculture in Nordic Countries 1987;129–30.

30. Balcázar JL, Vendrell D, Blas ID, Ruiz-Zarzuela I, Múzquiz JL. Effect of *Lactococcus lactis* CLFP 100 and *Leuconostoc mesenteroides* CLFP 196 on *Aeromonas salmonicida* infection in brown trout (*Salmo trutta*). Journal of Molecular Microbiology and Miotechnology 2009;17:153–7.

31. Kumagai A, Sugimoto K, Itou D, Kamaishi T, Miwa S, Iida T. *Atypical Aeromonas salmonicida* infection in cultured marbled sole *Pleuronectes yokohamae*. Fish Pathology 2006;41:7–12.

32. Pedersen K, Larsen JL. First report on outbreak of furunculosis in turbot *Scophthalmus maximus* caused by *Aeromonas salmonicida* subsp. *salmonicida* in Denmark. Bulletin of the European Association of Fish Pathologists 1996;16:129–33.

33. Reddy TV, Ravindranath K, Sreeraman PK, Rao MV. *Aeromonas salmonicida* associated with mass mortality of *Cyprinus carpio* and *Oreochromis mossambicus* in a freshwater reservoir in Andhra Pradesh, India. Journal of Aquaculture in the Tropics 1994;9:259–68.

34. Ilardi P, Avendaño-Herrera R. Isolation of *Flavobacterium*-like bacteria from diseased salmonids cultured in Chile. Bulletin of the European Association of Fish Pathologists 2008;28:176–85.

35. Ilardi P, Fernandez J, Avendano-Herrera R. *Chryseobacterium piscicola* sp. nov. isolated from diseased salmonid fish. International Journal of Systematic and Evolutionary Microbiology 2009;59:3001–5.

36. Chen MF, Kumlin ME. Enteric septicemia of channel catfish in California USA. California Fish and Game 1989;75:141–7.

37. Jarboe HH, Bowser PR, Robinette HR. Pathology associated with a natural *Edwardsiella ictaluri* infection in channel catfish (*Ictalurus punctatus* Rafinesque). Journal of Wildlife Diseases 1984;20:352–4.

38. Wagner BA, Wise DJ, Khoo LH, Terhune JS. The epidemiology of bacterial diseases in food-size channel catfish. Journal of Aquatic Animal Health 2002;14:263–72.

39. Ye S, Li H, Qiao G, Li Z. First case of *Edwardsiella ictaluri* infection in China farmed yellow catfish *Pelteobagrus fulvidraco*. Aquaculture 2009;292:6–10.

40. Xiao J, Wang Q, Liu Q, Wang X, Liu H, Zhang Y. Isolation and identification of fish pathogen *Edwardsiella tarda* from mariculture in China. Aquaculture Research 2008;40:13–7.

41. Nougayrede P, Vuillaume A, Vigneulle M, Faivre B, Luengo S, Delprat J. First isolation of *Edwardsiella tarda* from diseased turbot (*Scophthalmus maximus*) reared in a sea farm in the Bay of Biscay. Bulletin of the European Association of Fish Pathologists 1994;14:128–9.

42. Matsuoka S, Nakai T. Seasonal appearance of *Edwardsiella tarda* and its bacteriophages in the culture farms of Japanese flounder. Fish Pathology 2004;39:145–52.

43. Kanai K, Tawaki S, Uchida Y. An ecological study of *Edwardsiella tarda* on a flounder farm. Fish Pathology 1988;23:41–7.

44. Shome R, Shome BR, Sarangi N, Bandyopadhyay AK. Etiological characterization of acute infectious abdominal dropsy outbreak affecting Indian major carp, *Cirrhinus mrigala* in South Andaman. Current Science (Bangalore) 1996;70:744–7.

45. Fuhrmann H, Bohm KH, Savvidis G, Schlotfeldt H. *Edwardsiella tarda* as a possible causative agent of a disease in catfish (*Silurus glanis*) and eel (*Anguilla anguilla*). Bulletin of the European Association of Fish Pathologists 1985;5:57–60.

46. Alcaide E, Herraiz S, Esteve C. Occurrence of *Edwardsiella tarda* in wild European eels *Anguilla anguilla* from Mediterranean Spain. Diseases of Aquatic Organisms 2006;73:77–81.

47. Iregui CA, Guarín M, Tibatá VM, Ferguson HW. Novel brain lesions caused by *Edwardsiella tarda* in a red tilapia (*Oreochromis* spp.). Journal of Veterinary Diagnostic Investigation 2012;24:446–9.

48. Saleh WD. Isolation and identification of *Edwardsiella tarda* from infected Nile tilapia fish "*Oreochromis niloticus*". Bulletin of Faculty of Agriculture, Cairo University 2005;56:839–46.

49. Li N, Guo H, Jiao R, Zhang S, Liu Z, Yao W, *et al.* Identification and pathogenicity of bacterial pathogens isolated in an outbreak on bacterial disease of *Ctenopharyngodon idellus*. Acta Hydrobiologica Sinica 2011;35:980–7.

50. Decostere A, Ducatelle R, Haesebrouck F. *Flavobacterium columnare* (*Flexibacter columnaris*) associated with severe gill necrosis in koi carp (*Cyprinus carpio* L). Veterinary Record 2002;150:694–5.

51. Decei P, Dascalescu P, Macoveschi I. Outbreak of columnaris disease in trout on a fish farm. Revista de Cresterea Animalelor 1985;35:46–51.

52. Rehulka J, Mraz O. Columnarosis in rainbow trout (*Salmo gairdneri* R.) in Czechoslovakia. Acta Veterinaria Brno 1982;51:125–37.

53. Morley NJ, Lewis JW. Consequences of an outbreak of columnaris disease (*Flavobacterium columnare*) to the helminth fauna of perch (*Perca fluviatilis*) in the Queen Mary reservoir, south-east England. Journal of Helminthology 2010;84:186–92.

54. Mohamed SG, Saleh WD. *Flavobacterium columnare* infection in cultured *Oreochromis niloticus*. Assiut Veterinary Medical Journal 2010;56:15–30.

55. Figueiredo HC, Klesius PH, Arias CR, Evans J, Shoemaker CA, Pereira DJ, *et al.* Isolation and characterization of strains of *Flavobacterium columnare* from Brazil. Journal of Fish Diseases 2005;28:199–204.

56. Wagner BA, Wise DJ, Khoo LH, Terhune JS. The epidemiology of bacterial diseases in food-size channel catfish. Journal of Aquatic Animal Health 2002;14:263–72.

57. Soltani M, Munday B, Carson J. Susceptibility of some freshwater species of fish to infection by *Cytophaga johnsonae*. Bulletin of the European Association of Fish Pathologists 1994;14:133–5.

58. Dalsgaard I, Madsen L. Bacterial pathogens in rainbow trout, *Oncorhynchus mykiss* (Walbaum), reared at Danish freshwater farms. Journal of Fish Diseases 2000;23:199–209.

59. Bustos PA, Calbuyahue J, Montaña J, Opazo B, Entrala P, Solervicens R. First isolation of *Flexibacter psychrophilus*, as causative agent of rainbow trout fry syndrome (RTFS), producing rainbow trout mortality in Chile. Bulletin of the European Association of Fish Pathologists 1995;15:162–4.

60. Ostland VE, Lumsden JS, MacPhee DD, Ferguson HW. Characteristics of *Flavobacterium branchiophilum*, the cause of salmonid bacterial gill disease in Ontario. Journal of Aquatic Animal Health 1994;6:13–26.

61. Jeffery KR, Stone D, Feist SW, Verner-Jeffreys DW. An outbreak of disease caused by *Francisella* sp. in Nile tilapia *Oreochromis niloticus* at a recirculation fish farm in the UK. Diseases of Aquatic Organisms 2010;91:161–5.

62. Ostland VE, Stannard JA, Creek JJ, Hedrick RP, Ferguson HW, Carlberg JM, *et al.* Aquatic *Francisella*-like bacterium associated with mortality of intensively cultured hybrid striped bass *Morone chrysops*×*M. saxatilis*. Diseases of Aquatic Organisms 2006;72:135–45.

63. Coyne R, Smith P, Dalsgaard I, Nilsen H, Kongshaug H, Bergh O, *et al.* Winter ulcer disease of post-smolt Atlantic salmon: an unsuitable case for treatment? Aquaculture 2006;253:171–8.

64. Coyne R, Bergh O, Samuelsen O, Andersen K, Lunestad BT, Nilsen H, *et al.* Attempt to validate breakpoint MIC values estimated from pharmacokinetic data obtained during oxolinic acid therapy of winter ulcer disease in Atlantic salmon (*Salmo salar*). Aquaculture 2004;238:51–66.

65. Marcu A, Marcu A, Nichita I, Herman V, Pascu C, Costinar L, *et al.* Studies in the first outbreak of vibriosis associated with pasteurelosis at Siberian sturgeon (*Acipenser baerii*) in the south-west region of Romania. Preliminary Report. Lucrari Stiintifice – Zootehnie si Biotehnologii, Universitatea de Stiinte Agricole si Medicina Veterinara a Banatului Timisoara 2010;43:36–9.

66. Huang H, Tu C, Chuang S, Hung H, Su J, Lin S. Pasteurellosis in reared hybrid striped bass (*Morone saxatilis*×*Morone chrysops*). Fish Pathology 2001;36:35–7.

67. Bakopoulos V, Peric Z, Rodger H, Adams A, Richards R. First report of fish pasteurellosis from Malta. Journal of Aquatic Animal Health 1997;9:26–33.

68. Baptista T, Romalde JL, Toranzo AE. First occurrence of pasteurellosis in Portugal affecting cultured gilthead seabream (*Sparus aurata* [*Pagrus aurata*]). Bulletin of the European Association of Fish Pathologists 1996;16:92–5.

69. Toranzo AE, Barreiro S, Casal JF, Figueras A, Magarinos B, Barja JL. Pasteurellosis in cultured gilthead seabream (*Sparus aurata*): first report in Spain. Aquaculture 1991;99:1–15.

70. Fukuda Y. Studies on humoral immune response of yellowtail [*Seriola quinqueradiata*] against pseudotuberculosis. Bulletin

of Oita Institute of Marine and Fisheries Science (Japan) 1997;1:15–87.

71. Candan A, Ang Kucker M, Karatas S. Pasteurellosis in cultured sea bass (*Dicentrarchus labrax*) in Turkey. Bulletin of the European Association of Fish Pathologists 1996;16:150–3.

72. Tung M, Tsai S, Ho L, Huang S, Chen S. An acute septicemic infection of *Pasteurella* organism in pond-cultured Formosa snake-head fish (*Channa maculata* Lacepede) in Taiwan. Fish Pathology 1985;20:143–8.

73. Mladineo I, Miletic I, Bocina I. *Photobacterium damselae* subsp. *piscicida* outbreak in cage-reared Atlantic bluefin tuna *Thunnus thynnus*. Journal of Aquatic Animal Health 2006;18:51–4.

74. Liu P, Lin J, Lee K. Virulence of *Photobacterium damselae* subsp. *piscicida* in cultured cobia *Rachycentron canadum*. Journal of Basic Microbiology 2003;43:499–507.

75. Gaggero A, Castro H, Sandino AM. First isolation of *Piscirickettsia salmonis* from coho salmon, *Oncorhynchus kisutch* (Walbaum), and rainbow trout, *Oncorhynchus mykiss* (Walbaum), during the freshwater stage of their life cycle. Journal of Fish Diseases 1995;18:277–9.

76. Mauel MJ, Miller DL, Frazier K, Liggett AD, Styer L, Montgomery-Brock D, *et al.* Characterization of a piscirickettsiosis-like disease in Hawaiian tilapia. Diseases of Aquatic Organisms 2003;53:249–55.

77. Iregui CA, Vasquez GM, Rey AL, Verjan N. Piscirickettsia-like organisms as a cause of acute necrotic lesions in Colombian tilapia larvae. Journal of Veterinary Diagnostic Investigation 2011;23:147–51.

78. Ibrahem MD, Hatem ME. Mass mortality caused by *Pseudomonas fluorescens* and *Cryptocaryon irritans* in gilthead sea bream (*Sparus aurata* L.) in Egyptian mariculture. In: Proceedings of the Second Global Fisheries and Aquaculture Research Conference; 2009. p. 275–89.

79. Altinok I, Balta F, Capkin E, Kayis S. Disease of rainbow trout caused by *Pseudomonas luteola*. Aquaculture 2007;273:393–7.

80. Haenen OL, Davidse A. First isolation and pathogenicity studies with *Pseudomonas anguilliseptica* from diseased European eel *Anguilla anguilla* (L.) in The Netherlands. Aquaculture 2001;196:27–36.

81. Saeed MO, Alamoudi MM, Al-harbi AH. A *Pseudomonas* associated with disease in cultured rabbitfish *Siganus rivulatus* in the Red Sea. Diseases of Aquatic Organisms 1987;3:177–80.

82. Gatti R, Nigrelli DA. Haemorrhagic septicaemia in catfish. Pathogenicity of the strains isolated and reproducibility of the disease. Obiettivi e Documenti Veterinari 1984;5:61–3.

83. Woldemariam K, Dear G, Mochaba FM, Stewart DJ. An outbreak of 'Sekiten-byo' among cultured European eels, *Anguilla anguilla* L., in Scotland. Journal of Fish Diseases 1983;6:75–6.

84. Soltani M, Ahmadi MR, Yavari H, Mirzargar SS. Red-pink colony-producing *Pseudomonas sp*. is the causative agent of mass mortality in larvae and post-larvae of *Litopenaeus vannamei* raised in hatcheries in south Iran. International Journal of Veterinary Research 2010;4:89–94.

85. Hatai K, Egusa S, Nakajima M, Chikahata H. *Pseudomonas chlororaphis* as a fish pathogen. Bulletin of the Japanese Society of Scientific Fisheries 1975;41:1203.

86. Vilar P, Failde LD, Bermudez R, Vigliano F, Riaza A, Silva R, *et al.* Morphopathological features of a severe ulcerative disease outbreak associated with *Tenacibaculum maritimum* in cultivated sole, *Solea senegalensis* (L.). Journal of Fish Diseases 2012;35:437–45.

87. Avendano-Herrera R, Magarinos B, Irgang R, Toranzo AE. Use of hydrogen peroxide against the fish pathogen *Tenacibaculum maritimum* and its effect on infected turbot (*Scophthalmus maximus*). Aquaculture 2006;257:104–10.

88. Zhang F, Peng Z, Zhang J, Liu M, Fu R, Luo H. Isolation and identification of the pathogenic strain of *Vibrio harveyi* from *Miichthys miiuy*. Weishengwu Xuebao 2010;50:304–9.

89. Won KM, Kim KH, Park SI. *Vibrio harveyi* associated with deep skin ulcer in river puffer, *Takifugu obscures*, exhibited in a public aquarium. Aquaculture Research 2009;40:963–7.

90. Lin Y, Lin H. Analyses the biology and pathogenesis of virulence *Vibrio* spp. in grouper's aquaculture and the development vaccines for application. Journal of the Fisheries Society of Taiwan 2009;36:147–8.

91. Rodger HD, Colquhoun DJ. Clinical vibriosis in farmed Atlantic cod (*Gadus morhua*) in Ireland. Veterinary Record 2008;162:94–5.

92. Soumya H, Shruti C, Asakura M, Manambrakat V, Yamasaki S. Isolation of *Vibrio parahaemolyticus* and *Vibrio cholerae* (Non-O1 and O139) from moribund shrimp (*Penaeus monodon*) and experimental challenge study against post larvae and juveniles. Annals of Microbiology 2007;57:55–60.

93. Sakai T, Hirae T, Yuasa K, Kamaishi T, Matsuyama T, Miwa S, *et al.* Mass mortality of cultured kuruma prawn *Penaeus japonicus* caused by *Vibrio nigripulchritudo*. Fish Pathology 2007;42:141–7.

94. Yiagnisis M, Vatsos IN, Kyriakou C, Alexis M. First report of *Vibrio anguillarum* isolation from diseased big scale sand smelt, *Atherina boyeri* Risso 1810, in Limnos, Greece. Bulletin of the European Association of Fish Pathologists 2007;27:61–9.

95. Sakai T, Yamada H, Shimizu H, Yuasa K, Kamaishi T, Oseko N, *et al.* Characteristics and pathogenicity of brown pigment-producing *Vibrio anguillarum* isolated from Japanese flounder [*Paralichthys olivaceus*]. Fish pathology (Japan) 2006;41:77–9.

96. Cai J, Han Y, Wang Z. Isolation of *Vibrio parahaemolyticus* from abalone (*Haliotis diversicolor supertexta* L.) post larvae associated with mass mortalities. Aquaculture 2006;257:161–6.

97. Tanrikul TT. Outbreaks of *Vibrio alginolyticus* in gilthead sea bream in Turkey. Indian Veterinary Journal 2006;83:599–601.

98. Rasheed V. Vibriosis outbreak among cultured seabream (*Acanthopagrus cuvieri*) broodstock in Kuwait. Aquaculture 1989;76:189–98.

99. Fan W, Huang J, Wang X, Shi C, Liu L. Identification and phylogenetic study of pathogenic bacteria causing ulcer disease of cultured turbot (*Scophthalmus maximus*). Weishengwu Xuebao 2005;45:665–70.

100. Austin B, Stobie M, Robertson PA, Glass HG, Stark JR, Mudarris M. *Vibrio alginolyticus*: the cause of gill disease leading to progressive low-level mortalities among juvenile

turbot, *Scophthalmus maximus* L., in a Scottish aquarium. Journal of Fish Diseases 1993;16:277–80.

101. Zorrilla I, Arijo S, Chabrillon M, Diaz P, Martinez-Manzanares E, Balebona MC, *et al*. *Vibrio* species isolated from diseased farmed sole, *Solea senegalensis* (Kaup), and evaluation of the potential virulence role of their extracellular products. Journal of Fish Diseases 2003;26:103–8.

102. Liu P, Chuang W, Lee K. Infectious gastroenteritis caused by *Vibrio harveyi* (*V. carchariae*) in cultured red drum, *Sciaenops ocellatus*. Journal of Applied Ichthyology 2003;19:59–61.

103. Rajan PR, Lopez C, Lin JH, Yang H. *Vibrio alginolyticus* infection in cobia (*Rachycentron canadum*) cultured in Taiwan. Bulletin of the European Association of Fish Pathologists 2001;21:228–34.

104. Dalsgaard I, Hoi L, Siebeling RJ, Dalsgaard A. Indole-positive *Vibrio vulnificus* isolated from disease outbreaks on a Danish eel farm. Diseases of Aquatic Organisms 1999;35:187–94.

105. Biosca EG, Amaro C, Esteve C, Alcaide E, Garay E. First record of *Vibrio vulnificus* biotype 2 from diseased European eel, *Anguilla anguilla* L. Journal of Fish Diseases 1991;14:103–10.

106. Nicholson JT, Dodge P. Cold water vibriosis in Shetland salmon. Veterinary Record 1995;137:444.

107. Yashima T, Odajima T. An outbreak of vibriosis in wild ayu (*Plecoglossus altivelis*) and characteristics of the isolates. Journal of the Japan Veterinary Medical Association 1992;45:203–6.

108. Farkas J, Malik SE. Vibrio disease of sheatfish (*Silurus glanis* L.) fry. Aquaculture 1986;51:81–8.

109. Lewis DH. Vibriosis in channel catfish, *Ictalurus punctatus* (Rafinesque). Journal of Fish Diseases 1985;8:539–45.

110. Guguianu E, Vulpe V, Lazar M, Rîmbu C. Yersiniosis outbreak in rainbow trout (*Oncorhynchus mykis*) at a fish farm from northern Romania. Cercetari Agronomice în Moldova 2009;42:75–80.

111. Oraic D, Zrnčic S, Šoštaric B, Bazulic D, Lipej Z. Occurrence of enteric redmouth disease in rainbow trout (*Oncorhynchus mykiss*) in farms in Croatia. Acta Veterinaria Hungarica 2002;50:283–91.

112. Rodríguez LA, Castillo A, Gallardo CS, Nieto TP. Outbreaks of *Yersinia ruckeri* in rainbow trout in north west of Spain. Bulletin of the European Association of Fish Pathologists 1999;19:130–2.

113. Eissa AE, Moustafa M, Abdelaziz M, Ezzeldeen NA. *Yersinia ruckeri* infection in cultured Nile tilapia, *Oreochromis niloticus*, at a semi-intensive fish farm in lower Egypt. African Journal of Aquatic Science 2008;33:283–6.

114. Dear G. *Yersinia ruckeri* isolated from Atlantic salmon in Scotland. Bulletin of the European Association of Fish Pathologists 1988;8:18–20.

115. Sparboe O, Håsteom T, Poppe TT, Koren C, Stenwig H. *Yersinia ruckeri* infection in salmon demonstrated for the first time in Norway. Norsk Veterinaertidsskrift 1986;98:189–92.

116. Park K, Matsuoka S, Nakai T, Muroga K. A virulent bacteriophage of *Lactococcus garvieae* (formerly *Enterococcus seriolicida*) isolated from yellowtail *Seriola quinqueradiata*. Diseases of Aquatic Organisms 1997;29:145–9.

117. Schmidtke LM, Carson J. *Lactococcus garvieae* strains isolated from rainbow trout and yellowtail in Australia, South Africa and Japan differentiated by repetitive sequence markers. Bulletin of the European Association of Fish Pathologists 2003;23:206–12.

118. Soltani M, Nikbakht G, Mousavi HA, Ahmadzadeh N. Epizootic outbreaks of lactococcosis caused by *Lactococcus garvieae* in farmed rainbow trout (*Oncorhynchus mykiss*) in Iran. Bulletin of the European Association of Fish Pathologists 2008;28:207–12.

119. Chang PH, Lin CW, Lee YC. *Lactococcus garvieae* infection of cultured rainbow trout, *Oncorhynchus mykiss*, in Taiwan and associated biophysical characteristics and histopathology. Bulletin of the European Association of Fish Pathologists 2002;22:319–27.

120. Aguado-Urda M, Lopez-Campos GH, Gibello A, Teresa Cutuli M, Lopez-Alonso V, Fernandez-Garayzabal JF, *et al.* Genome sequence of *Lactococcus garvieae* 8831, isolated from rainbow trout lactococcosis outbreaks in Spain. Journal of Bacteriology 2011;193:4263–4.

121. Kobayashi T, Ishitaka Y, Imai M, Kawaguchi Y. Pathological studies on *Lactococcus garvieae* infection of cultured rockfish *Sebastes schlegeli*. Suisanzoshoku (Japan) 2004;52:359–64.

122. Lee J, Chu S, Yu Z, Lee C, Lai C, Hung C, *et al.* Identification and survey on gram-positive *Streptococcus*-like organisms isolated from grey mullet (*Mugil cephalus* Linnaeus). Taiwan Veterinary Journal 2006;32:136–45.

123. Wang PC, Chen SD, Tsai MA, Weng YJ, Chu SY, Chern RS, *et al. Nocardia seriolae* infection in the three striped tigerfish, *Terapon jarbua* (Forsskål). Journal of Fish Diseases 2009;32:301–10.

124. Wang G, Xu Y, Jin S, Zhu J, Zhu W. Research on the nocardiosis and pathogen in reared snakehead, *Ophiocephalus argus* Cantor. Acta Hydrobiologica Sinica 2009;33:277–83.

125. Wang G, Xu Y, Jin S, Zhu J, Yuan S. Nocardiosis in snakehead, *Ophiocephalus argus* Cantor. Aquaculture 2007;271:54–60.

126. Wang G, Yuan S, Jin S. Preliminary study on nocardiosis in cage-reared large croaker, *Pseudosciaena crocea* (Richardson). Journal of Fisheries of China 2006;30:103–7.

127. Wang G, Yuan S, Jin S. Nocardiosis in large yellow croaker, *Larimichthys crocea* (Richardson). Journal of Fish Diseases 2005;28:339–45.

128. Huang S, Lai K, Su S, Shei M, Chen S. Isolation and characterization of the pathogenic bacterium, *Nocardia seriolae*, from female broodstock of striped mullet (*Mugil cephalus*). Journal of Taiwan Fisheries Research 2004;12:61–9.

129. Chen S, Lee J, Lai C, Gu Y, Wang C, Chang H, *et al.* Nocardiosis in seabass, *Lateolabrax japonicu*s, in Taiwan. Journal of Fish Diseases 2000;23:299–307.

130. Chen S. The study on the pathogenicity of *Nocardia asteroides* to largemouth bass *Micropterus salmoides* Lacepede. Fish Pathology 1992;27:1–5.

131. Chen SC, Tung MC. An epizootic in large mouth bass (*Micropterus salmoides* Lacepede), caused by *Nocardia asteroides* in fresh water pond in southern Taiwan. Journal of the Chinese Society of Veterinary Science 1991;17:15–22.

132. Kitao T, Ruangpan L, Fukudome M. Isolation and classification of a *Nocardia* species from diseased giant gourami *Osphronemus goramy*. Journal of Aquatic Animal Health 1989;1:154–62.

133. Kusuda R, Nakagawa A. Nocardial infection of cultured yellowtail. Fish Pathology 1978;13:25–31.

134. Lorenzen E, Olesen NJ, Korsholm H, Heuer OE, Evensen O. First demonstration of *Renibacterium salmoninarum*/BKD in Denmark. Bulletin of the European Association of Fish Pathologists 1997;17:140–4.

135. Evensen O, Dale OB, Nilsen A. Immunohistochemical identification of *Renibacterium salmoninarum* by monoclonal antibodies in paraffin-embedded tissues of Atlantic salmon (*Salmo salar* L.), using paired immunoenzyme and paired immunofluorescence techniques. Journal of Veterinary Diagnostic Investigation 1994;6:48–55.

136. Hatakeyama M, Miura K. Seasonal change in serum agglutination titer against *Renibacterium salmoninarum* in farmed masu salmon *Oncorhynchus masou*. Scientific Reports of the Hokkaido Fish Hatchery (Japan) 2006;60:91–7.

137. Gil P, Vivas J, Gallardo CS, Rodriguez LA. First isolation of *Staphylococcus warneri*, from diseased rainbow trout, *Oncorhynchus mykiss* (Walbaum), in northwest Spain. Journal of Fish Diseases 2000;23:295–8.

138. Huang S, Chen W, Shei M, Liao I, Chen S. Studies on epizootiology and pathogenicity of *Staphylococcus epidermidis* in Tilapia (*Oreochromis* spp.) cultured in Taiwan. Zoological Studies 1999;38:178–88.

139. Wang W, Chang Y, Shieh M, Lin C. *Staphylococcus epidermidis* and cestode infection of cultured grass carp (*Ctenopharyngodon idella*) in Taiwan. Reports on Fish Disease Research 1996;0:57–63.

140. Wang W, Shieh M, Lee J, Liu C. Case report: *Staphylococcus epidermidis* isolated from diseased cultured sea perch (*Lateolabrax japonicus*) in Taiwan. Taiwan Journal of Veterinary Medicine and Animal Husbandry 1995;65:305–9.

141. Baxa DV, Kawai K, Ando H, Kusuda R. *Edwardsiella tarda* and *Staphylococcus aureus* isolated from cultured red sea bream. Reports of the USA Marine Biological Institute Kochi University 1985;7:1–8.

142. Kusuda R, Sugiyama A. Studies on the characters of *Staphylococcus epidermidis* isolated from diseased fish. I. Morphological, biological and biochemical properties. Fish Pathology 1981;16:15–24.

143. Ye X, Li J, Lu M, Deng G, Jiang X, Tian Y, *et al.* Identification and molecular typing of *Streptococcus agalactiae* isolated from pond-cultured tilapia in China. Fisheries Science 2011;77:623–32.

144. Abuseliana AF, Daud HH, Aziz SA, Bejo SK, Alsaid M. Pathogenicity of *Streptococcus agalactiae* isolated from a fish farm in Selangor to juvenile red tilapia (*Oreochromis* sp.). Journal of Animal and Veterinary Advances 2011;10:914–9.

145. Bowater RO, Forbes-Faulkner J, Anderson IG, Condon K, Robinson B, Kong F, *et al.* Natural outbreak of *Streptococcus agalactiae* (GBS) infection in wild giant Queensland grouper, *Epinephelus lanceolatus* (Bloch), and other wild fish in northern Queensland, Australia. Journal of Fish Diseases 2012;35:173–86.

146. Glibert PM, Landsberg JH, Evans JJ, Al-Sarawi MA, Faraj M, Al-Jarallah MA, *et al.* A fish kill of massive proportion in Kuwait Bay, Arabian Gulf, 2001: the roles of bacterial disease, harmful algae, and eutrophication. Harmful Algae 2002;1:215–31.

147. Al-Marzouk A, Duremdez R, Al-Gharabally H. Efforts to control outbreaks of diseases among cultured silver pomfret *Pampus argenteus* in Kuwait. Journal of Aquaculture in the Tropics 2004;19:103–10.

148. Pasnik DJ, Evans JJ, Klesius PH, Shoemaker CA, Yeh, H. Pathogenicity of *Streptococcus ictaluri* to channel catfish. Journal of Aquatic Animal Health 2009;21:184–8.

149. Al Harbi AH. Molecular characterization of *Streptococcus iniae* isolated from hybrid tilapia [*Oreochromis niloticus*×*Oreochromis aureus*]. Aquaculture 2011;312:15–8.

150. El Aamri F, Padilla D, Acosta F, Caballero MJ, Roo J, Bravo J, *et al.* First report of *Streptococcus iniae* in red porgy (*Pagrus pagrus* L.). Journal of Fish Diseases 2010;33:901–5.

151. Haghighi Karsidani S, Soltani M, Nikbakhat-Brojeni G, Ghasemi M, Skall H. Molecular epidemiology of zoonotic streptococcosis/lactococcosis in rainbow trout (*Oncorhynchus mykiss*) aquaculture in Iran. Iranian Journal of Microbiology 2010;2:198–209.

152. Ozaki A, Okamoto H, Yamada T, Matuyama T, Sakai T, Fuji K, *et al.* Linkage analysis of resistance to *Streptococcus iniae* infection in Japanese flounder (*Paralichthys olivaceus*). Aquaculture 2010;308:S62–7.

153. Creeper JH, Buller NB. An outbreak of *Streptococcus iniae* in barramundi (*Lates calcarifera*) in freshwater cage culture. Australian Veterinary Journal 2006;84:408–11.

154. Yuasa K, Kitancharoen N, Kataoka Y, Al-Murbaty FA. *Streptococcus iniae*, the causative agent of mass mortality in rabbitfish *Siganus canaliculatus* in Bahrain. Journal of Aquatic Animal Health 1999;11:87–93.

155. Stoffregen DA, Backman SC, Perham RE, Bowser PR, Babish JG. Initial disease report of *Streptococcus iniae* infection in hybrid striped (Sunshine) bass and successful therapeutic intervention with the fluoroquinolone antibacterial enrofloxacin. Journal of the World Aquaculture Society 1996;27:420–34.

156. Kaige N, Miyazaki T, Kubota SS. The pathogen and histopathoglogy of vertebral deformaity in cultured yellowtail *Seriola quinqueradiata*. Fish Pathology 1984;19:173–80.

157. Chen D, Wang K, Geng Y, Wang J, Huang L, Li J. *Streptococcus iniae* isolated from channel catfish (*Ictalurus punctatus*) in China. Israeli Journal of Aquaculture Bamidgeh 2011;63:593.

158. Yang W, Li A. Isolation and characterization of *Streptococcus dysgalactiae* from diseased Acipenser schrenckii. Aquaculture 2009;294:14–7.

159. Nomoto R, Unose N, Shimahara Y, Nakamura A, Hirae T, Maebuchi K, *et al.* Characterization of Lancefield group C *Streptococcus dysgalactiae* isolated from farmed fish. Journal of Fish Diseases 2006;29:673–82.

160. Nomoto R, Munasinghe LI, Jin D, Shimahara Y, Yasuda H, Nakamura A, *et al.* Lancefield group C *Streptococcus dysgalactiae* infection responsible for fish mortalities in Japan. Journal of Fish Diseases 2004;27:679–86.

161. Domenech A, Fernandez-Garayzabal JF, Pascual C, Garcia JA, Cutuli MT, Moreno MA, *et al. Streptococcosis in cultured turbot, Scophthalmus maximus* (L.), associated with

Streptococcus parauberis. Journal of Fish Diseases 1996;19:33–8.

162. Han SY, Kang BK, Kang BJ, Kim JM, Han JE, Kim JH, *et al.* Protective efficacy of a combined vaccine against *Edwardsiella tarda*, *Streptococcus iniae* and *Streptococcus parauberis* in farmed olive flounder *Paralichthys olivaceus*. Fish Pathology 2011;46:108–11.

163. Romalde JL, Ravelo C, Valdés I, Magariños B, Fuente ED, San MC, *et al. Streptococcus phocae*, an emerging pathogen for salmonid culture. Veterinary Microbiology 2008;130:198–207.

164. Ruiz-Zarzuela I, de Blas I, Girones O, Ghittino C, Muzquiz JL. Isolation of *Vagococcus salmoninarum* in rainbow trout, *Oncorhynchus mykiss* (Walbaum), broodstocks: characterization of the pathogen. Veterinary Research Communications 2005;29:553–62.

165. Michel C, Nougayrede P, Eldar A, Sochon E, De Kinkelin P. *Vagococcus salmoninarum*, a bacterium of pathological significance in rainbow trout *Oncorhynchus mykiss* farming. Diseases of Aquatic Organisms 1997;30:199–208.

166. Figueiredo HC, Costa FA, Leal CA, Carvalho-Castro GA, Leite RC. *Weissella* sp. outbreaks in commercial rainbow trout (*Oncorhynchus mykiss*) farms in Brazil. Veterinary Microbiology 2012;156:359–66.

167. Liu J, Li A, Ji C, Yang W. First description of a novel *Weissella* species as an opportunistic pathogen for rainbow trout *Oncorhynchus mykiss* (Walbaum) in China. Veterinary Microbiology 2009;136:314–20.

168. Wei Q. Social and economic impacts of aquatic animal health problems in aquaculture in China. FAO Fisheries Technical Paper 2002;406:55–61.

169. Cunha BA. Antibiotic resistance. Medical Clinics of North America 2009;84:1407–29.

170. Defoirdt T, Boon N, Sorgeloos P, Verstraete W, Bossier P. Alternatives to antibiotics to control bacterial infections: luminescent vibriosis in aquaculture as an example. Trends in Biotechnology 2007;25:472–9.

171. Defoirdt T, Sorgeloos P, Bossier P. Alternatives to antibiotics for the control of bacterial disease in aquaculture. Current Opinion in Microbiology 2011;14:251–8.

172. Chinabut S, Puttinaowarat S. The choice of disease control strategies to secure international market access for aquaculture products. Developments in Biologicals Progress in Fish Vaccinology 2005;121:255–61.

173. Sommerset I, Krossøy B, Biering E, Frost P. Vaccines for fish in aquaculture. Expert Review of Vaccines 2005;4:89–101.

174. Fang HM, Ge R, Sin YM. Cloning, characterisation and expression of *Aeromonas hydrophila* major adhesin. Fish and Shellfish Immunology 2004;16:645–58.

175. Håstein T, Gudding R, Evensen O. Bacterial vaccines for fish – an update of the current situation worldwide. Developments in Biologicals (Basel) 2005;121:55–74.

176. Park SI. Disease control in Korean aquaculture. Gyobyo Kenkyu=Fish Pathology 2009;44:19–23.

177. Faisal M, Popp W, Refai M. *Aeromonas hydrophila*-related septicemia in the Nile tilapia *Oreochromis niloticus*. Berliner und Münchener Tierärztliche Wochenschrift 1989;102:87–93.

178. Pathiratne A, Widanapathirana GS, Chandrakanthi WHS. Association of *Aeromonas hydrophila* with epizootic ulcerative syndrome (EUS) of freshwater fish in Sri Lanka. Journal of Applied Ichthyology, 1994;10:204–8.

179. Yambot AV. Isolation of *Aeromonas hydrophila* from *Oreochromis niloticus* during fish disease outbreaks in the Philippines. Asian Fisheries Science 1998;10:347–54.

180. Nielsen ME, Høi L, Schmidt AS, Qian D, Shimada T, Shen JY, *et al.* Is *Aeromonas hydrophila* the dominant motile *Aeromonas* species that causes disease outbreaks in aquaculture production in the Zhejiang Province of China? Diseases of Aquatic Organisms 2001;46:23–9.

181. Xia C, Ma Z, Rahman H, Wu Z. PCR Cloning and identification of the b-hemolysin gene of *Aeromonas hydrophila* from freshwater fishes in China. Aquaculture 2004;229:45–53.

182. Pridgeon JW, Klesius PH. Molecular identification and virulence of three *Aeromonas hydrophila* isolates cultured from infected channel catfish during a disease outbreak in West Alabama in 2009. Diseases of Aquatic Organisms 2011;94:249–53.

183. Pridgeon JW, Klesius PH. Virulence of *Aeromonas hydrophila* in the presence or absence of extracellular products to channel catfish fingerlings. Diseases of Aquatic Organisms 2011;95:209–15.

184. Ruangpan L, Kitao T, Yoshida T. Protective efficacy of *Aeromonas hydrophila* vaccines in Nile tilapia. Veterinary Immunology and Immunopathology 1986;12:345–50.

185. Chandran MR, Aruna BV, Logambal SM, Michael RD. Immunisation of Indian major carps against *Aeromonas hydrophila* by intraperitoneal injection. Fish and Shellfish Immunology 2002;13:1–9.

186. John MB, Chandran MR, Aruna BV, Anbarasu K. Production of superoxide anion by head-kidney leucocytes of Indian major carps immunised with bacterins of *Aeromonas hydrophila*. Fish and Shellfish Immunology 2002;12:201–7.

187. Guan R, Xiong J, Huang W, Guo S. Enhancement of protective immunity in European eel (*Anguilla anguilla*) against *Aeromonas hydrophila* and *Aeromonas sobria* by a recombinant *Aeromonas* outer membrane protein. Acta Biochimica et Biophysica Sinica 2011;43:79–88.

188. Poobalane S, Thompson KD, Ardó L, Verjan N, Han HJ, Jeney G, *et al.* Production and efficacy of an *Aeromonas hydrophila* recombinant S-layer protein vaccine for fish. Vaccine 2010;28:3540–7.

189. Khushiramani R, Girisha SK, Karunasagar I, Karunasagar I. Protective efficacy of recombinant OmpTS protein of *Aeromonas hydrophila* in Indian major carp. Vaccine 2007;25:1157–8.

190. LaPatra SE, Plant KP, Alcorn S, Ostland V, Winton J. An experimental vaccine against *Aeromonas hydrophila* can induce protection in rainbow trout, *Oncorhynchus mykiss* (Walbaum). Journal of Fish Diseases 2010;33:143–51.

191. Hernanz Moral C, Flaño del Castillo E, López Fierro P, Villena Cortés A, Anguita Castillo J, Cascón Soriano A, *et al.* Molecular characterization of the *Aeromonas hydrophila aroA* gene and potential use of an auxotrophic *aroA* mutant as a live attenuated vaccine. Infection and Immunity 1998;66:1813–21.

192. Liu Y, Bi Z. Potential use of a transposon Tn916-generated mutant of *Aeromonas hydrophila* J-1 defective in some exoproducts as a live attenuated vaccine. Preventive Veterinary Medicine 2007;78:79–84.

193. Khashe S, Hill W, Janda JM. Characterization of *Aeromonas hydrophila* strains of clinical, animal, and environmental origin expressing the O:34 antigen. Current Microbiology 1996;33:101–8.

194. Bernardet J, Vancanneyt M, Matte-Tailliez O, Grisez L, Tailliez P, Bizet C, *et al.* Polyphasic study of *Chryseobacterium* strains isolated from diseased aquatic animals. Systematic and Applied Microbiology 2005;28:640–60.

195. Algoet M. Project FC1151 – Risks to public health and the aquaculture industry associated with bacterial fish diseases and their treatment. Trout News 2004;38:23–3.

196. Kamaishi T, Fukuda Y, Nishiyama M, Kawakami H, Matsuyama T, Yoshinaga T, *et al.* Identification and pathogenicity of intracellular *Francisella* bacterium in three-line grunt *Parapristipoma trilineatum*. Fish Pathology 2005;40:67–71.

197. Ostland VE, Stannard JA, Creek JJ, Hedrick RP, Ferguson HW, Carlberg JM, *et al.* Aquatic *Francisella*-like bacterium associated with mortality of intensively cultured hybrid striped bass *Morone chrysops*×*M.* saxatilis. Diseases of Aquatic Organisms 2006;72:135–45.

198. Olsen AB, Mikalsen J, Rode M, Alfjorden A, Hoel E, Straum-Lie K, *et al.* A novel systemic granulomatous inflammatory disease in farmed Atlantic cod, *Gadus morhua* L., associated with a bacterium belonging to the genus *Francisella*. Journal of Fish Diseases 2006;29:307–11.

199. Nylund A, Ottem KF, Watanabe K, Karlsbakk E, Krossoy B. *Francisella* sp. (Family *Francisellaceae*) causing mortality in Norwegian cod (*Gadus morhua*) farming. Archives of Microbiology 2006;185:383–92.

200. Ottem KF, Nylund A, Isaksen TE, Karlsbakk E, Bergh O. Occurrence of *Francisella piscicida* in farmed and wild Atlantic cod, *Gadus morhua* L., in Norway. Journal of Fish Diseases 2008;31:525–34.

201. Mauel MJ, Soto E, Moralis JA, Hawke J. A piscirickettsiosis-like syndrome in cultured Nile tilapia in Latin America with *Francisella* spp. as the pathogenic agent. Journal of Aquatic Animal Health 2007;19:27–34.

202. Soto E, Hawke JP, Fernandez D, Morales JA. *Francisella* sp., an emerging pathogen of tilapia, *Oreochromis niloticus* (L.), in Costa Rica. Journal of Fish Diseases 2009;32:713–22.

203. Soto E, Baumgartner W, Wiles J, Hawke JP. *Francisella asiatica* as the causative agent of piscine francisellosis in cultured tilapia (*Oreochromis* sp.) in the United States. Journal of Veterinary Diagnostic Investigation 2011;23:821–5.

204. Birkbeck TH, Bordevik M, Froystad MK, Baklien A. Identification of *Francisella* sp. from Atlantic salmon, *Salmo salar* L., in Chile. Journal of Fish Diseases 2007;30:505–7.

205. Kamaishi T, Miwa S, Goto E, Matsuyama T, Oseko N. Mass mortality of giant abalone *Haliotis gigantea* caused by a *Francisella* sp. bacterium. Diseases of Aquatic Organisms 2010;89:145–54.

206. Hsieh CY, Tung MC, Tu C, Chang CD, Tsai SS. Enzootics of visceral granulomas associated with *Francisella*-like organism infection in tilapia (*Oreochromis* spp.). Aquaculture 2006;254:129–38.

207. Ellingsen T, Inami M, Gjessing MC, Van Nieuwenhove K, Larsen R, Seppola M, *et al. Francisella noatunensis* in Atlantic cod (*Gadus morhua* L.); waterborne transmission and immune responses. Fish and Shellfish Immunology 2011;31:326–33.

208. Soto E, Wiles J, Elzer P, Macaluso K, Hawke JP. Attenuated *Francisella asiatica* iglC mutant induces protective immunity to francisellosis in tilapia. Vaccine 2011;29:593–8.

209. Wakabayashi H, Egusa S. Characteristics of a *Pseudomonas* sp. from an epizootic of pond-cultured eels (*Anguilla japonica*). Bulletin of the Japanese Society of Scientific Fisheries 1972;38:577–87.

210. Wiklund T, Bylund G. *Pseudomonas anguilliseptica* as a pathogen of salmonid fish in Finland. Diseases of Aquatic Organisms 1990;8:13–20.

211. Domenech A, Fernandez-Garayzabal JF, Lawson P, Garcia JA, Cutuli MT, Blanco M, *et al.* Winter disease outbreak in sea-bream (*Sparus aurata*) associated with *Pseudomonas anguilliseptica* infection. Aquaculture 1997;156:317–26.

212. Doménech A, Fernández-Garayzábal JF, García JA, Cutuli MT, Blanco M, Gibello A, *et al.* Association of *Pseudomonas anguilliseptica* infection with 'winter disease' in sea bream, *Sparus aurata* [*Pagrus aurata*] L. Journal of Fish Diseases 1999;22:69–71.

213. Nakai T, Muroga K. Studies on red spot disease of pond-cultured eels. V. Immune response of the Japanese eel to the causative bacterium *Pseudomonas anguilliseptica*. Bulletin of the Japanese Society of Scientific Fisheries 1979;45:817–21.

214. Muroga K, Ohnishi K, Jo Y, Tanimoto H, Nakai T. Studies on red spot disease of pond-cultured eels. IX. A field vaccination trial. Aquaculture 1982;30:131–5.

215. Romalde JL, Ravelo C, Lopez-Romalde S, Avendalo-Herrera R, Magarinos B, Toranzo AE. Vaccination strategies to prevent emerging diseases for Spanish aquaculture. Developments in Biologicals Progress in Fish Vaccinology 2005;121:85–95.

216. Cui Q, Wang L, Huang Y, Liu Z, Goodfellow M. *Nocardia jiangxiensis* sp. nov. and *Nocardia miyunensis* sp. nov., isolated from acidic soils. International Journal of Systematic and Evolutionary Microbiology 2005;55:1921–5.

217. Yamamura H, Tamura T, Sakiyama Y, Harayama S. *Nocardia amamiensis* sp. nov., isolated from a sugar-cane field in Japan. International Journal of Systematic and Evolutionary Microbiology 2007;57:1599–602.

218. Xing K, Qin S, Fei SM, Lin Q, Bian GK, Miao Q, *et al. Nocardia endophytica* sp. nov., an endophytic actinomycete isolated from the oil-seed plant *Jatropha curcas* L. International Journal of Systematic and Evolutionary Microbiology 2011;61:1854–8.

219. Olubunmi PA, Ayeni AO. A description of an outbreak of bovine nocardiosis in Western Nigeria. Journal of Animal Production Research 1983;3:127–38.

220. Javadi M, Kanavi MR, Zarei-Ghanavati S, Zarei S, Mirbabaei F, Jamali H, *et al.* Outbreak of *Nocardia keratitis* after photorefractive keratectomy: clinical, microbiological, histopathological, and confocal scan study. Medical trials and studies. Journal of Cataract and Refractive Surgery 2009;35:393–8.

221. Darzi MM, Mir MS, Nashiruddullah N, Kamil SA. Nocardiosis in domestic pigeons (*Columba livia*). Veterinary Record 2006;158:834–6.

222. Sahathevan M, Harvey FA, Forbes G, O'grady J, Gimson A, Bragman S, *et al.* Epidemiology, bacteriology and control of

an outbreak of *Nocardia asteroides* infection on a liver unit. Journal of Hospital Infection 1991;18:473–80.

223. Shimahara Y, Yasuda H, Nakamura A, Itami T, Yoshida T. Detection of antibody response against *Nocardia seriolae* by enzyme-linked immunosorbent assay (ELISA) and a preliminary vaccine trial in yellowtail *Seriola quinqueradiata*. Bulletin of the European Association of Fish Pathologists 2005;25:270–5.

224. Shimahara Y, Huang Y, Tsai M, Wang P, Chen S. Immune response of largemouth bass, *Micropterus salmoides*, to whole cells of different *Nocardia seriolae* strains. Fisheries Science (Tokyo) 2010;76:489–94.

225. Itano T, Kawakami H, Kono T, Sakai M. Live vaccine trials against nocardiosis in yellowtail *Seriola quinqueradiata*. Aquaculture 2006;261:1175–80.

226. Edwards AM, Massey RC, Clarke SR. Molecular mechanisms of *Staphylococcus aureus* nasopharyngeal colonization. Molecular Oral Microbiology 2012;27:1–10.

227. Diekema DJ, Pfaller MA, Schmitz FJ, Smayevsky J, Bell J, Jones RN, *et al.* Beach, M. Survey of infections due to *Staphylococcus* species: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, Latin America, Europe, and the Western Pacific region for the SENTRY Antimicrobial Surveillance Program, 1997–1999. Clinical Infectious Diseases 2001;32:S114–32.

228. Shah KL, Tyagy BC. An eye disease in silver carp, *Hypophthalmichthys molitrix*, held in tropical ponds, associated with the bacterium *Staphylococcus aureus*. Aquaculture 1986;55:1–4.

229. Heath PT. An update on vaccination against group B streptococcus. Expert Review of Vaccines 2011;10:685–94.

230. Zdragas A, Tsakos P, Kotzamanidis C, Anatoliotis K, Tsaknakis I. Outbreak of mastitis in ewes caused by *Streptococcus agalactiae*. Deltion tes Ellenikes Kteniatrikes Etaireias [Journal of the Hellenic Veterinary Medical Society] 2005;56:114–21.

231. Watts JL, Nickerson SC, Pankey JW. A case study of *Streptococcus* group G infection in a dairy herd. Veterinary Microbiology 1984;9:571–80.

232. Evans JJ, Klesius PH, Gilbert PM, Shoemaker CA, Al-Sarawi MA, Landsberg J, *et al*. Characterization of β-haemolytic Group B *Streptococcus agalactiae* in cultured seabream, *Sparus auratus* L., and wild mullet, *Liza klunzingeri* (Day), in Kuwait. Journal of Fish Diseases 2002;25:505–13.

233. Evans JJ, Klesius PH, Shoemaker CA. Efficacy of *Streptococcus agalactiae* (group B) vaccine in tilapia (*Oreochromis niloticus*) by intraperitoneal and bath immersion administration. Vaccine 2004;22:3769–73.

234. Pasnik DJ, Evans JJ, Klesius PH. Duration of protective antibodies and correlation with survival in Nile tilapia *Oreochromis niloticus* following *Streptococcus agalactiae* vaccination. Diseases of Aquatic Organisms 2005;66:129–34.

235. Manjaiang P, Areechon N, Srisapoome P, Mahasawas S. Application of vaccine to prevent disease caused by *Streptococcus agalactiae* in Nile tilapia (*Oreochromis niloticus*). Proceedings of the 45th Kasetsart University Annual Conference 2007;174–82.

236. Sheehan B, Labrie L, Lee Y, Lim W, Wong F, Chan J, *et al.* Streptococcal diseases in farmed tilapia. Aquaculture Asia Pacific 2009;5:26–9.

237. Perera RP, Johnson SK, Collins MD, Lewis DH. *Streptococcus iniae* associated with mortality of *Tilapia nilotica*×*T. aurea* hybrids. Journal of Aquatic Animal Health 1994;6:335–40.

238. Eldar A, Horovitcz A, Bercovier H. Development and efficacy of a vaccine against *Streptococcus iniae* infection in farmed rainbow trout. Veterinary Immunology and Immunopathology 1997;56:175–83.

239. Bercovier H, Ghittino C, Eldar A. Immunization with bacterial antigens: infections with streptococci and related organisms. Developments in Biological Standardization 1997;90:153–60.

240. Eyngor M, Tekoah Y, Shapira R, Hurvitz A, Zlotkin A, Lublin A, Eldar A. Emergence of novel *Streptococcus iniae* exopolysaccharide-producing strains following vaccination with nonproducing strains. Applied and Environmental Microbiology 2008;74:6892–7.

241. Bachrach G, Zlotkin A, Hurvitz A, Evans DL, Eldar A. Recovery of *Streptococcus iniae* from diseased fish previously vaccinated with a streptococcus vaccine. Applied and Environmental Microbiology 2001;67:3756–8.

242. Klesius PH, Shoemaker CA, Evans JJ. Efficacy of a killed *Streptococcus iniae* vaccine in tilapia (*Oreochromis niloticus*). Bulletin of the European Association of Fish Pathologists 1999;19:39–41.

243. Klesius PH, Shoemaker CA, Evans JJ. Efficacy of single and combined *Streptococcus iniae* isolate vaccine administered by intraperitoneal and intramuscular routes in tilapia (*Oreochromis niloticus*). Aquaculture 2000;188:237–46.

244. Klesius PH, Evans JJ, Shoemaker CA, Pasnik DJ. A vaccination and challenge model using calcein marked fish. Fish and Shellfish Immunology 2006;20:20–8.

245. Shoemaker CA, Vandenberg GW, Désormeaux A, Klesius PH, Evans JJ. Efficacy of a *Streptococcus iniae* modified bacterin delivered using Oralject™ technology in Nile tilapia (*Oreochromis niloticus*). Aquaculture 2006;255:151–6.

246. Locke JB, Aziz RK, Vicknair MR, Nizet V, Buchanan JT. *Streptococcus iniae* M-like protein contributes to virulence in fish and is a target for live attenuated vaccine development. Public Library of Science One 2008;3:e2824.

247. Buchanan JT, Stannard JA, Lauth X, Ostland VE, Powell HC, Westerman ME, Nizet V. *Streptococcus iniae* phosphoglucomutase is a virulence factor and a target for vaccine development. Infection and Immunity 2005;73:6935–44.

248. Pridgeon JW, Klesius PH. Development and efficacy of a novobiocin-resistant *Streptococcus iniae* as a novel vaccine in Nile tilapia (*Oreochromis niloticus*). Vaccine 2011;29:5986–93.